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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/804,014 | 03/12/2001 | Li Li | 15966-721 | 8877 |

30623 7590 09/21/2004

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| EXAMINER | |
|---|---|
| SULLIVAN, DANIEL M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1636 | |

DATE MAILED: 09/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/804,014 | LI ET AL. | |
| | Examiner | Art Unit | |
| | Daniel M Sullivan | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *5,9,10,12-14,30,33 and 44-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,9,10,12-14,30,33 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

This Office Action is a reply to the Paper filed 16 June 2004 in response to the Non-Final Office Action mailed 16 January 2004. Claims 5, 9, 10, 12-14, 30, 33 and 44-46 were considered in the 16 January Office Action. Claim 14 was amended in the 16 June Paper. Claims 5, 9, 10, 12-14, 30, 33 and 44-46 are presently pending and under consideration.

### *Response to Amendment and Arguments*

Claim Rejections - 35 USC § 102

Rejection of claims 5, 12-14, 30 and 33 under 35 U.S.C. 102(b) as being anticipated by NCBI online, Accession No. AC008687 is withdrawn in view of Applicant's arguments and the sequence alignment provided as Exhibit 1.

Claim 10 stands rejected under 35 U.S.C. 102(b) as being anticipated by NCBI online, Accession No. AC008687 for reasons of record. Applicant argues that the nucleic acid of claim 10 is limited to hybridizing under stringent conditions to the nucleotide sequence of SEQ ID NO: 7 and is therefore not anticipated by the art. This argument has been fully considered but is not deemed persuasive because, as pointed out in the previous Office Action, the sequence disclosed in AC008687 comprises regions having substantial identity with the instant SEQ ID NO: 7. Therefore, absent evidence to the contrary, the skilled artisan would conclude that the AC008687 sequence would hybridize to SEQ ID NO: 7 under stringent conditions.

Claim Rejections - 35 USC § 101

Rejection of claim 14 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of the amendments thereto.

Claim Rejections - 35 USC § 112

Claims 5, 9, 10, 12-14, 30, 33 and 44-46 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons of record and herein below in the response to Applicant arguments.

The claims were rejected on the grounds that the specification fails to teach the skilled artisan how to use the claimed nucleic acid as asserted in the specification without undue experimentation.

In response to the *prima facie* case of record, Applicant first alleges that the rejection under 35 U.S.C. §112, first paragraph, is in reality a *de facto* utility rejection and that the reasons provided for rejecting the claims all relate back to whether the asserted utilities for the claimed nucleic acid are proven specific and credible. Applicant urges that, because the claims are not rejected under 35 U.S.C. §101 as lacking a specific and substantial credible utility, a rejection under 35 U.S.C. §112, first paragraph, should not be imposed.

This argument is not deemed persuasive. "If an applicant has disclosed a specific and substantial utility for an invention and provided a credible basis supporting that utility, that fact alone does not provide a basis for concluding that the claims comply with all the requirements of 35 U.S.C. 112, first paragraph." MPEP 2164.07. As stated in the previous Office Action, "the specification fails to teach the skilled artisan how to use the nucleic acid for the specific and

substantial credible utilities set forth in the specification without undue experimentation" (page 5). This conclusion is based on a careful analysis of the disclosure according to the factual inquiries set forth in *In re Wands* (CA FC) 8 USPQ2d 1400. Thus, the rejection is clearly based on the requirements of 35 U.S.C. §112, first paragraph, and not 35 U.S.C. §101.

Applicant next asserts that the teachings of the specification do, in fact, enable at least one of the asserted uses, namely, to identify compounds that modulate the Kv channel. Applicant urges that the specification describes screening assays that can be used to identify molecules that can be used to modulate the functions of the claimed polypeptide and cites other disclosures of methods of identifying molecules that modulate functions of an ion-channel as evidence that such assays were known in the art. Applicant argues that one of skill in the art can readily perform cell-based assays to identify molecules that can modify the functions of the potassium channel.

This argument has been fully considered but is not deemed persuasive because even if one were able to identify a modulator of the channel, the specification fails to provide an enabled use for the modulator. As discussed in the previous Office Action, the only asserted utility for the reagents developed using the claimed invention is therapeutic, yet the specification provides no specific guidance as to how the agents developed with the invention can be used therapeutically. All of the teachings in the specification related to therapy are general in nature and based on circumstantial evidence. Therefore, the skilled artisan seeking to use the claimed invention therapeutically or in the identification or production of therapeutics would have to engage in undue experimentation to first identify a disease that could be treated, develop an effective therapeutic agent and then develop an effective treatment regimen. This degree of

experimentation is clearly beyond what is considered routine in the art. Therefore, the skilled artisan would not be able to use the claimed invention without undue experimentation.

Applicant asserts that all members of the Kv family share the common utility of transporting potassium ions. However, this is neither a specific nor substantial utility because there are a wide variety of proteins capable of transporting potassium ions, each of which will have a distinct utility based on the unique properties of the protein. For example, one would not assert that the sodium-potassium ATPase, the target of cardiac glycosides used in treating heart disease, has the same specific and substantial utility as the stomach hydrogen-potassium ATPase, which is the target for agents used to treat gastroesophageal reflux disease. Thus, an assertion that a protein is capable of transporting potassium ions is not a specific and substantial asserted utility.

Applicant next cites Kalman *et al.* (1998) *J. Biol. Chem* 273:5851-5857 as teaching a mouse polypeptide having some structural similarity to the protein encoded by the instant nucleic acid which is expressed in heart, skeletal muscle and pancreatic islet cells, and a protein mapped to a disease locus. Applicant asserts that it is well known in the art at the time that potassium channels are involved in neuromuscular disorders. Applicant also cites art indicating that another protein related to the *Drosophila* Shaker family of $K^+$ channels is expressed in pancreatic islets and insulinomas. Applicant concludes from this that, "it is clear to a person skilled in the art that the NOV4 polypeptide is involved in the transport of potassium ions and that the NOV4 polypeptide is associated with pathologies including diabetes mellitus and neuromuscular disorders such as acquired neuromyotonia."

These arguments have been fully considered but are not deemed persuasive. Applicant appears to be asserting that teachings from the art establish a role for the polypeptide encoded by the claimed nucleic acid in diabetes mellitus and acquired neuromyotonia such that the skilled artisan could use the claimed invention to identify modulators which could then be used to treat diabetes mellitus and neuromuscular disorders without undue experimentation. As discussed at length in the previous Office Action, the art recognizes that polypeptides having the structure of a voltage gated potassium channel could play a role in any one of a variety of physiological or pathological conditions and that, given the state of the art even as of 2002 (when Wickenden was published), one of ordinary skill would not know what the physiological or pathological function of a polypeptide would be based only on its structural similarity to the family of voltage gated potassium channels. The art cited by Applicant is no more enabling for the claimed nucleic acid than is the specification itself. Although Kalman *et al.* speculates that the potassium channel described therein "may contribute at least one subunit to hetromulitimeric Kv channels in pancreatic β cells" (paragraph bridging the left and right columns on page 5856) the skilled artisan would not know how to treat diabetes mellitus using a modulator of the protein Kalman *et al.* is actually referring to, let alone a modulator of any protein having limited structural similarity to that protein. In fact, before one could use the claimed invention to develop modulators as potential therapeutics to treat diabetes mellitus it would have to establish that the polypeptide plays a role in the disease, which would require undue empirical experimentation.

Likewise, Vincent *et al.* (2000) *Eur. J. Biochem.* 267 :6717-6728, cited by applicant as teaching that potassium channels are involved in neuromuscular disorders, teaches that the voltage gated potassium channel or channels responsible for neuromyotonia has not yet been

established (see especially the first full paragraph on page 6724). Therefore, again the skilled artisan would have to establish what, if any, role the polypeptide encoded by the claimed invention played in neuromyotonia, or any other neuromuscular disorder, by empirical experimentation before one could reasonably use the invention to screen for potential therapeutics for those conditions.

As discussed in the previous Office Action, the asserted utilities for the claimed nucleic acid appear to be based on its encoding a polypeptide that is likely a voltage gated potassium channel and physiological functions established for other members of the family. However, the art teaches that there are many different proteins belonging to the family of voltage gated potassium channels. These proteins are expressed in different tissues and are involved in various physiological and path physiological processes. Given this functional diversity, the skilled artisan would be unable to use the claimed nucleic acid, or other reagents developed therefrom, for the utilities asserted in the specification without first engaging in empirical experimentation to establish a nexus between the functioning of the NOV4 protein and some physiological or pathological state. This degree of experimentation is clearly beyond what is considered routine in the art. Therefore, the skilled artisan would not be able to use the claimed invention without undue experimentation.

Applicant's arguments have been fully considered but are not deemed persuasive either individually or as a whole. Therefore, the claims stand rejected under 35 U.S.C. §112, first paragraph, as lacking an enabling disclosure.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M Sullivan, Ph.D.
Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER